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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,302	05/01/2002	Daniel R. Dietrich	MBP-010XX	2837

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EXAMINER	
CEPERLEY, MARY	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,302	DIETRICH ET AL.	
	Examiner	Art Unit	
	Mary (Molly) E. Ceperley	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2004 and 13 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12 and 14-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12 and 14-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2) Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

3) Claims 1, 3-12 and 14-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The claims are again rejected for the reason set forth in paragraph ***4)d)*** of the September 03, 2003 Office action. Applicants' statement in the paragraph bridging pages 14 and 15 of the March 03, 2004 response that "an ordinary skilled artisan would know which groups would be appropriate to make a cyclic moiety" does not serve to clarify and establish the exact structure of the "cyclic moiety". It is unclear what an "appropriate" cyclic structure would be. Further, applicants' have not addressed the question of whether the "cyclic structure" is meant to include the microcystin-specific antibodies of Nagata et al wherein the hapten contains a cyclic heptapeptide moiety, which might appear to be an "appropriate" cyclic structure given the specific field of the invention.

b) In claim 1, it is unclear what the phrase "when bound to nitrogen" modifies.

c) In dependent claim 4, the term "acylamino" is broader than the term "(C_1 – C_4) acylamino" in independent claim 1.

d) The addition of "R^2" defined as "glutamidyl" or "2-aminoproprionamidyl" (sic) in claim 1 appear to be inappropriate since the paragraph bridging pages 5 and 6 of the specification indicates that these definitions are *subsets* of the earlier recited definitions of "R^2" of claim 1 ("(C_1-C_4) acylamino"?). Applicants must clarify what is intended by the terms

"glutamidyl" and "2-aminoproprionamidyl" and how they relate to the earlier definitions of "R^2" which appear in claim 1. See also, claim 19.

e) Claims 16 and 27 are confusing and incomplete for the following reasons.

i) The term "group represented by the formula (I)" is undefined. See also, claims 9 and 28.

ii) The chemical nature and function of "a second compound" are undefined rendering the claim indefinite.

iii) The use of the term "reaction" (implying a chemical reaction" is confusing since it would appear that specific binding between a hapten and its corresponding antibody is occurring .

iv) It is unclear whether the method of claim 16 is directed to the detection of a hapten or its corresponding antibody ("method for detecting a compound containing the group represented by the formula (I)").

v) The claim is incomplete in not reciting a step of adding a sample containing the moiety to be detected, a step of forming a hapten-antibody complex and a step wherein the detection of the complex is related to the presence/amount of antibody (or hapten?) in the sample.

f) In claim 19 the use of the alternative term "or" to define specific subsets of "compounds" appears to be incorrect and is confusing for the reasons that the first appearing definition "group R^1 represents acylamino and group R^2 represents (C_1-C_4) acyl" appears to *encompass* the two subsequent definitions of the combinations of "R^1" and "R^2".

g) Claims 21 and 22 are confusing for the reason that it involves a "method for the preparation of the compound according to claim 19", which is itself *the binding site of an antibody* (see claim 1), but the recited method steps involve the preparation of *an immunogen*.

h) In claim 28, there is no antecedent basis for the term "formula (I)".

4) Claim 22 is objected to as being a duplicate of claim 21.

5) Claims 9-11 are rejected under 35 U.S.C. 112, first paragraph, for the reason set forth in paragraph ***7)*** of the first Office action. Applicants' arguments filed March 03, 2003 (Remarks, last paragraph of page 15) have been fully considered but they are not persuasive. Contrary to applicants' statement, the method of claim 9 *requires* the preparation of the *immunogen* which, of necessity, requires the conjugation of an immunogenic carrier to the hapten. Therefore the problems noted in paragraph ***7)*** of the first Office action still apply.

6) Claims 1 and 3-9 are rejected under 35 U.S.C. 102(b)/103(a) as being anticipated or obvious over each of ***a)*** Nagata et al (Natural Toxins (1995)) or An et al (Toxicon (1994)) for the reasons set forth in paragraph ***12)*** of the first Office action.

Applicants' arguments filed March 03, 2003 have been fully considered but they are not persuasive. Applicants argue that the antibodies of the prior art differ from those of the instant claims for the reason that the antibodies of the prior art "were all raised against complete microcystin-LR (MC-LR) molecules and not against the isolated ADDA group" and as a consequence, "each of the antibodies contains a binding site for an epitope *which may overlap with the ADDA moiety* but which also interacts with other groups present in complete MC-LR" (emphasis added). The antibodies of the instant invention, on the other hand, are stated to be specific for the ADDA moiety described in formula (I) of instant claim 1 and therefore different from the prior art antibodies.

This argument regarding antibody specificity relies on *the structure of the specific hapten used to prepare the immunogen*. However, the antibodies of instant claim 1 *are not limited to antibodies prepared using the specific ADDA hapten*. Rather, the antibodies of instant claim 1 must only *be reactive with* an epitope comprised of an ADDA hapten. The prior art antibodies prepared from haptens which contain the ADDA moiety are considered to be functionally equivalent to the antibodies of instant claim 1, i.e. both the prior art and claimed antibodies have "a binding site" for the ADDA moiety. It is further

noted that the antibodies of claim 1 which bind to compounds of formula (I) wherein "R1 and R2 are connected to each other to form a cyclic moiety" appear to be directly readable on the prior art antibodies which are prepared using the entire MC-LR structure as a hapten, i.e. the compounds of formula (I) wherein "R^1 and R^2 are connected to each other to form a cyclic moiety" would include MC-LR.

The Dietrich declaration is directed to antibodies *prepared from* "the isolated ADDA group coupled to a carrier". However, as noted above, the antibodies of claim 1 do not require the use of isolated ADDA for their preparation; the antibodies of claim 1 are limited to those antibodies which provide "a binding site" for the ADDA moiety but there is no requirement that they be *produced from* an isolated ADDA-moiety. Thus, the data presented in the declaration, related to the improved cross-reactivity characteristics of antibodies produced from an isolated-ADDA happen are not commensurate in scope with the claimed subject matter and therefore do not overcome the prior art rejections of record.

7) Claims 10-12 and 14-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagata et al (Natural Toxins (1995)) or An et al (Toxicon (1994)) for the reasons set forth in paragraph ***13)*** of the first Office action. The statements made in paragraph ***6)*** above apply to this rejection as well.

8) Claims 1, 3-12 and 14-28 are again rejected under 35 U.S.C. 103(a) as being unpatentable over ***a)*** Nagata et al (Natural Toxins (1995)) or An et al (Toxicon (1994)) taken alone or in combination with ***b)*** Humphrey et al (JACS (1996)) for the reasons stated in paragraph ***11)*** of the first Office action.

The statements made in paragraph ***6)*** above apply as well to this rejection. It is again emphasized that the antibodies of instant claim 1 *are not limited to antibodies prepared using the specific ADDA hapten*. For the claim 9 method of preparing an antibody, it is noted that that the hapten used to prepare the immunogen must "contain" the ADDA moiety ("containing a group represented by formula (I)") but the hapten is not *limited to* the ADDA moiety *per se*. Both the claimed and prior art antibodies have a binding site for an ADDA-containing moiety.

9) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10) An inquiry of a general nature which is ***not related to the prosecution on the merits*** should be directed to Technology Center 1600 telephone number (571) 272-1600. The general fax number for the USPTO is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (571) 272-0813. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (571) 272-0823.

June 25, 2004

Mary E. Ceperley

Mary (Molly) E. Ceperley
Primary Examiner
Art Unit 1641